LABORATORY DIAGNOSIS IN THE EARLY STAGES OF CONGENITAL SYPHILIS.

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In some recent work which I have been doing it has occurred to me that many cases of latent congenital syphilis have been overlooked. This has occurred, it has seemed, because of the general tendency of most physicians to regard a positive or negative Wassermann as of far greater importance than any physical findings. Those most familiar with the Wassermann reaction are least likely to take this exaggerated view of its usefulness. The above statements probably apply more to the first few weeks of life than to any other period. It seems to me to be of use, therefore, to examine carefully into the various laboratory methods which may be used to further our knowledge before the appearance of such active symptoms as will make all such tests unnecessary.

It should be said in starting that either clinicians have gone very far astray in their judgment of what constitutes congenital syphilis in this period or else the laboratory tests are to a certain extent very misleading. Rietschel[1] says: "These children before the outbreak of an exanthem neither clinically, serologically, nor cytologically show the slightest sign of a lues." By most French clinicians the presence of an enlarged spleen is regarded as most suggestive of luetic taint at this period, and when this is combined with a history of syphilis in the parents and the presence of epitrochlear glands one may feel a strong suspicion at least that a luetic condition exists.

The following body fluids are frequently examined with an idea to ascertaining the nature of a disturbance in the early weeks of life:

Urine.
Blood.
Cerebrospinal fluid.

Urine. There is very little of diagnostic value to be found in the urine of a luetic infant. While it is true that in many of these cases at autopsy a chronic inflammatory condition of the kidney is to be found, still, as a rule, this does not show clinically. At best the clinical findings in a case of nephritis at this age would be confusing, especially in the first days of life when albuminuria from other cause is comparatively frequent.

Blood. Routine examination of the blood shows conditions that vary markedly in the first few weeks of life, and especially the first few days. This should make us skeptical about interpreting findings at this time which would seem to point to syphilis. Lymphocytosis, or rather the predominance of mononuclear lymphocytes, is a normal finding at this age, and the variation of 5 per cent. or even 10 one way or the other is of sufficient frequency in cases other than syphilitic to be of little value from a diagnostic stand-point. The number of leukocytes is so variable that any decrease or increase within the limits which would be expected in congenital syphilis makes comparatively little difference in differentiating the condition.

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[1] Med. Klinik, 1909, v, 658.

We come now to the question of the value of the Wassermann reaction in these cases. It seems to be a well-established fact that in over 90 per cent. of clinically certain cases of congenital syphilis the Wassermann reaction is positive. This, however, tells us little. We know so little about the true reason for the appearance of the Wassermann reaction that the interpretation of such a finding is not as evident as it may appear. One would think that if all cases of congenital syphilis positive clinically give a positive Wassermann reaction, that then all cases of congenital syphilis should do the same; and while this may be true to a greater or less extent, still the occurrence of a florid syphilis probably means the presence in the blood of those bodies which are most likely to produce a positive Wassermann. The absence of such bodies from the blood, so far as our present knowledge goes, does not by any means exclude the presence of an active syphilis. The findings of Rietschel[2] and of Ledermann[3] prove the usefulness of the Wassermann in cases of congenital syphilis. They do not account for such conditions, however, as are recorded by Halberstädter, E. Müller, and Reiche[4] in scarlet fever where temporarily at least a positive Wassermann reaction was obtained in five of ten cases, nor in another of their cases where syphilis developed after a negative Wassermann had been obtained. Nor do they account for such cases as those of Cassoute,[5] who obtained different reactions in twins, nor of Niemann,[6] who gives the account of a peculiar form of disease as yet not classified in which the Wassermann reaction was distinctly positive. We may say from this, therefore, that while in the active stages of the disease a positive Wassermann is of distinct value, the negative is of comparatively little, since many cases of syphilis unquestionably exist in which the blood gives no positive Wassermann reaction. But even a positive Wassermann reaction may go astray, as in the case reported by Niemann. It would be well now to look into the condition of affairs as they exist in the newborn infant and in the first few weeks of life. Most German authorities have satisfied themselves with the statement that sufficient data is not present to draw any positive conclusions as to the value of the Wassermann reaction at this stage. The subject, however, has been exhaustively treated by Bar and Daunay.[7] The examination carried on by these investigators was made on the blood from the umbilicus[8] of fifty-seven newborn infants, the blood being tested immediately after birth. These cases were divided into four groups:

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[2] Loc. cit.

[3] Arch. f. Derm. u. Syph., 1911, cvi, 325.

[4] Berl. klin. Woch., 1908, xlv, 1917.

[5] Bull. de la Soc. de Péd. de Paris, 1913, xv, 179.

[6] Jahrb. f. Kinderheilk, 1914, lxxix, 1.

Group 1. Fourteen born of mothers with florid syphilis.

Group 2. Eleven born of mothers with syphilitic symptoms, not of a florid type.

Group 3. Fourteen born of mothers with suspected syphilis.

Group 4. Eighteen born of mothers well or apparently well.

Bar and Daunay distinguish four reactions: (1) The strongly positive, (2) the partially positive, (3) doubtful, and (4) negative. In Group 1:2, or 14.28 per cent., were positive; 1, or 7.14 per cent., partial; 6, or 42.84 per cent., doubtful, and 5, or 35.71 per cent., negative. In Group 2:2, or 22.22 per cent., were positive, while 7, or 78.78 per cent., were negative. In Group 3:4, or 28.51 per cent., were positive; 1, or 17.04 per cent., partial, 2, or 14.28 per cent., doubtful, and 7, or 50 per cent., negative. Of the children in Group 4, 6 were examined immediately after birth. Of these, 1, or 16.66 per cent., gave partial reaction, 1, or 16.66 per cent., doubtful, and 4, or 66.66 per cent., negative. Of 12 children that were examined somewhat later 2, or 16.66 per cent., gave positive Wassermann; 1, or 18.08 per cent., partial; 4, or 33.33 per cent., doubtful, and 5, or 41.66 per cent., negative. From these statistics they draw the following conclusions:

1. The method of Wassermann does not necessarily give concordant results in the mother and her infant.
2. Of 34 cases there has been agreement only 16 times, or 46.53 per cent.
3. The agreement is less where the maternal syphilis is florid (4 times in 14 cases, or 38.57 per cent.) than in the cases where the maternal syphilis is old or non-florid, 12 times in 20 cases, or 60 per cent.
4. In the majority of cases where there has been agreement the result has been negative in both mother and infant.
5. When there has been disagreement it is shown to be more often positive in the mother (9 in 18 cases).

Further, there is an analysis of 13 infants born of mothers with syphilis or a condition which was at least strongly suspicious and who gave negative reactions. Of these 1 showed no signs of syphilis later; 9 presented unquestioned syphilitic lesions; and of the 3 who died, 1 was distinctly syphilitic, and 1 a monster. Bar and Daunay state that the positive result in the newborn has the same significance as that in the mother, but that the significance of partial or doubtful reactions is greater in the newborn probably because of biliary pigments in the blood.

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[7] L'Obstétrique, 1909, ii, 1, 192, 260.

[8] Exceptions are noted below.

CEREBROSPINAL FLUID. The routine examination of cerebrospinal fluid at this period brings some interesting but not conclusive evidence. The globulin content as estimated by the Nonné or Noguchi tests while giving positive reaction in a certain proportion of cases certainly does not do this in all, even in the active stages, so that while the evidence of a positive reaction is suggestive it is by no means conclusive, and even when present may signify the presence of other conditions than congenital syphilis. The cell content is practically always increased, though this too is subject to wide variation, so much so that Baron[9] concludes that no dependence can be put upon the number of the cells present nor upon the differential count. There is a widespread opinion that in syphilis in general the number of cells is increased and the large proportion of these cells are mononuclear in type. While this holds good to a large extent in congenital syphilis, still the finding is not so general as to be of much value in differentiating the condition.

Recently, Lange has suggested a test by the use of a colloidal gold chloride solution in different dilutions of cerebrospinal fluid. This test was based on the fact that certain albuminous bodies when brought in contact with a solution of colloidal gold in the presence of an electrolyte would, in certain concentration, cause a clumping together of the smaller colloidal particles, producing various changes in color and even precipitation. This test was originally devised for the purpose of distinguishing tabes dorsalis and paretic dementia. By some it is held that this test represents merely a means of determining the presence of albuminous bodies in the cerebrospinal fluid, and hence is of little more value than are such tests as the Nonné and Noguchi. The theory on which the test is based is certainly contrary to this opinion, since the colloidal gold clumps at different dilutions with different albumin bodies, though at present it is not possible to state positively at just what dilutions certain albumin bodies produce this reaction. It seems to me that one can be readily convinced of a certain degree of specificity in this reaction if he will note the regularity with which the cerebrospinal fluids from certain conditions produce reaction in certain dilutions. With the idea of testing this reaction in congenital syphilis, Dr. Moody and myself[10] tested the cerebrospinal fluid of 9 cases of typical congenital syphilis, in every case of which reaction was strongest in the dilution of 1 to 40 and 1 to 80. In one case which was tested within six weeks and found positive, the reaction at thirteen weeks after seven weeks of treatment was negative. In many of these cases the Nonné test looked quite doubtful and the Wassermann on the cerebrospinal fluid was very frequently negative. In 7 cases of suspected congenital syphilis in all but one the same reaction held true. In one the reaction was the same as the one obtained in paretic dementia, the child died a few days after the removal of the fluid. Unfortunately no autopsy was obtained. In one the reaction was very weak and the subsequent course led one to think that the case if syphilitic at all had only a slight taint. Of these 14 cases only 3 came within the time mentioned as the doubtful period, but of these all 3 showed distinct positive reactions, and the course of the disease subsequently was altogether confirmatory of the presence of congenital syphilis. Of non-syphilitic cases there seems to be one type which is likely to give a reaction in the same dilution as does that of congenital syphilis. This is the meningismus or serous meningitis. In the two cases in our series affected with pneumonia complicated by meningimus or serous meningitis both gave the greatest reaction in dilutions of 1 to 40 and 1 to 80. In one of these, syphilis could not be absolutely ruled out. In the other one there was certainly no clinical evidence of the condition, and subsequent tests led us to think that this was a source of error. While the data at hand is too small to allow conclusions of a positive nature to be drawn, still the findings as brought out in this series of cases is distinctly suggestive, and it is possible that in the Lange test we have a means of confirming any suspicions which we may have of syphilis in the early months of life. The test is a very easy one to perform and may be carried out without much special equipment, provided the solution of colloidal gold chloride is prepared in a laboratory. While at first it was thought very difficult to prepare this, a little experience seems to have overcome these difficulties.

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[9] Jahrb. f. Kinderheilk. 1909, lxix, 25.

[10] Jour. Amer. Med. Assoc., 1913, lxi, 13.

The consideration of this subject would not be complete without taking into account the recently proposed luetin test of Noguchi.[11] With this test the writer has had very little experience, and hence must depend almost altogether upon the reports of Noguchi. Of these, for our purpose, comparatively few are useable. Of Holt's 33 cases 15 were between the ages of one and three months. Of these 12 were positive and 3 negative. All positive cases had been given mercuial treatment previous to the reaction, while the 3 negative cases had received no such treatment, 73 non-syphilitic cases gave negative reaction. The Noguchi luetin reaction, therefore, is in much the same state as is the gold chloride reaction. Both need much confirmatory evidence in order to affirm or deny their importance.

Conclusions. 1. There is no test which is proved to be pathognomonic of congenital syphilis in the early stages between the birth and the development of active symptoms.

2. The examination of the urine and the routine examination of cerebrospinal fluid for globulin content and cells offers little evidence of value for the diagnosis of this stage of the disease.

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[11] Serum Diagnosis of Syphilis, Philadelphia, 1912, 179.

3. The evidence as to the Wassermann reaction all goes to show the unreliability of the test at this age.

4. The Lange gold chloride reaction on the cerebrospinal fluid offers at present some hope that the evidence obtained in this way may be of distinct benefit.

5. So far as we may judge from the luetin test as at present reported active treatment with mercury materially influences it, so much so that without the mercurial treatments no cases have as yet proved positive. It may be said, however, that the Noguchi test has a distinctly negative value, inasmuch as in all cases not syphilitic the reaction was negative.

MODERN METHODS OF TREATMENT OF SYPHILIS OF THE NERVOUS SYSTEM.

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The discoveries of Schaudinn, Wassermann, Ehrlich, and Noguchi have led to great changes in the methods of diagnosis and of treatment of syphilitic disease of the central nervous system. Those of us who have enjoyed the privilege of testing these newer methods on a large number of hospital and private patients have also the duty of reporting the results obtained and the conclusions reached.

Omitting from present consideration all our earlier cases, we have the records of about 120 cases to form the basis of this study. It is no easy matter to arrive at just conclusions in a subject so full of pitfalls. The spontaneous remission and exacerbations of all syphilitic forms of central nervous disease make it particularly difficult to ascertain accurately the effect of any form of treatment. Hence the necessity of observing an impartial, critical attitude toward the newer remedies and methods applied to the treatment of these conditions.

We have included in the list of cases 55 cases of tabes, 20 of general paresis, 41 of cerebral and cerebrospinal lues, 3 of optic neuritis, and 2 of specific spondylitis.

Present Methods. Every patient admitted to our service in the hospital, especially if syphilitic disease of the nervous system is suspected, is subjected to a lumbar puncture for routine examination of the spinal fluid. A Wassermann test is made, using the fluid in quantities up to 1 c.c., according to the method of Hauptmann and Hoessli, and the cell count is estimated as soon as possible after the withdrawal of the spinal fluid. The Fuchs-Rosenthal